

## **II. REMARKS**

Claims 1 to 21 are pending. Applicants and Applicants' representative gratefully acknowledge the Examiner's attention to the case and the helpful suggestions made in the telephone interview held May 8, 2002.

### **A. Regarding the Amendment**

Claim 10 has been amended to correct a readily apparent typographical error. As such, the amendment does not add new matter.

### **B. Regarding Claims 1 to 9**

The rejection of claims 1 to 9 under 35 U.S.C. § 101 as allegedly lacking utility, and the objection to the specification and corresponding rejection of claims 1 to 9 under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement, are respectfully traversed.

Claims 1 to 9 are directed to compositions comprising an Mcl-1 gene regulatory element. In response to the previous Office Action, it was pointed that the specification discloses that an Mcl-1 gene regulatory element of the invention can be used, for example, as a tool for identifying an agent that can modulate expression of a nucleotide sequence operatively linked to the regulatory element (see page 47, line 1, to page 51, line 15), and that a regulatory element of the invention can be linked to a heterologous nucleic acid molecule, for example, for the purpose of co-expressing the heterologous nucleic acid molecule in a cell with endogenous Mcl-1 (see, for example, page 46, lines 18-26).

It is stated in the present Office Action that the use of the claimed Mcl-1 gene regulatory element to identify agents that regulate expression from the element is not a patentable utility because "it constitutes further experimentation regarding the activation of the regulatory element" (Office Action at page 2, paragraph 5). However, as discussed in the interview with the Examiner, the claimed Mcl-1 gene regulatory element is not a subject for further research, but is useful as a tool that allows the identification of agents that can modulate the activity of the regulatory element. It is submitted that use of the Mcl-1 regulatory element

in a screening assay is a specific utility because only the Mcl-1 gene regulatory element can be used to identify such agents. In addition, it is submitted that a screening assay is a substantial and credible utility because companies have been formed and provide services based on drug screening platforms. For example, as discussed with the Examiner, Idun Pharmaceuticals is a company that has developed drug screening platforms based on apoptotic pathways, and uses the drug screening assays to identify agents that can modulate apoptosis (see world wide web at "idun.com", then "Technology" link). Another example of a company that focuses on screening assays, particularly for identifying drugs that modulate gene expression is Genelabs Technologies, Inc. (see world wide web at "genelabs.com", then "Research and Development" link). As such, it is submitted that screening assays provide a real world value, as evidenced by the focus of various companies on providing such a service.

In summary, it is submitted that screening assays provide a patentable utility, and that no further experimentation regarding activation of the Mcl-1 gene regulatory element is required upon performing a screening assay as disclosed in the subject application. Accordingly, it is respectfully requested that the objection to the specification and the rejections of claims 1 to 9 under 35 U.S.C. § 101 and 35 U.S.C. § 112, first paragraph, be removed.

### **C. Regarding Claims 10 to 21**

The objection to the specification and corresponding rejection of claims 10 to 21 under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement are respectfully traversed.

Claims 10 to 13 are directed to polynucleotides encoding an Mcl-1 polypeptide, which has anti-apoptotic activity. Claims 14 to 19 are directed to polynucleotides encoding an alternatively spliced Mcl-1 polypeptide ( $\Delta$ Mcl-1), which has apoptotic activity. Claims 20 and 21 are directed to oligonucleotides, which are useful, for example, as probes for identifying Mcl-1 gene expression.

It is maintained in the Office Action that the specification provides no objective evidence that induction of Mcl-1 polypeptide in neurons would be sufficient to prevent the

neurons from undergoing apoptosis because Mcl-1 is expressed in hematopoietic cells, which are biochemically distinct from neurons. As discussed with the Examiner, however, the specification discloses that Mcl-1 is expressed in various cell types, including, for example, HepG2 hepatocytes and MCF-7 breast carcinoma cells (see page 75, lines 5-7; and page 79, line 30, to page 80, line 4). As further evidence that Mcl-1 is widely expressed in a variety of cell types, Applicants have submitted herewith as Exhibit B a reference by Krajewski et al. (*Am. J. Pathol.* 146:1309, 1995). Krajewski et al. report that Mcl-1 is expressed in epithelial cells, various neuroendocrine cells, and in some neuronal cells (see Abstract; see, also, Table 1 at page 1312; and page 1316, left column, first full paragraph). As such, it is clear that Mcl-1 is expressed in a wide variety of cell types.

It also is stated in the Office Action that there is no objective evidence that administration of SEQ ID NO:3, for example, to patients suffering from cancer would induce apoptosis of the cancer cells. As an initial matter, it is noted that the claims are directed to compositions and, therefore, any patentable utility is sufficient to meet the utility requirement. As such, Applicants submit that it is not necessary to show, for example, that administration of a polynucleotide encoding the  $\Delta$ Mcl-1 polypeptide to a patient results in apoptosis of cancer cells in the subject. Applicants point out, however, that the specification discloses that transfection of HeLa cells, which are derived from cervical carcinoma cells, with a polynucleotide encoding the apoptotic  $\Delta$ Mcl-1 polypeptide induced cell death in the HeLa cells (page 84, lines 11-18). As such, it is submitted that one skilled in the art, viewing the specification, would have known how to use a polynucleotide encoding, for example, the apoptotic  $\Delta$ Mcl-1 polypeptide to induce apoptosis in cells that otherwise would grow continuously in culture.

Furthermore, it is noted, for example, that the specification discloses that various cancers, including, for example, prostate cancer, can be treated using the compositions of the invention (see page 53, line 28, to page 54, line 2; see, also, page 53, lines 11-14). In this respect, Applicants point out that, after the filing of the subject application, it was reported that

Mcl-1 levels are increased in hyperplastic and carcinomatous prostate, as compared to normal prostate (see Royuela et al., *Eur. Cytokine Netw.* 12:654, 2001, which is attached as Exhibit C; see, for example, Abstract, and Table 1 at page 656). As such, it is submitted that, as disclosed in the specification, a pathological condition such as prostate cancer can be associated with aberrant expression of an Mcl-1 polypeptide and, therefore, abnormal levels of apoptosis (see, for example, page 53, lines 26-28).

With respect to claims 20 and 21, which are directed to oligonucleotides that can hybridize specifically to nucleotide sequences of a nucleic acid molecule encoding an Mcl-1 polypeptide, Applicants' representative noted in the interview that no specific arguments appear to have been made in support of the rejection of the claims. Nevertheless, it is submitted that one skilled in the art would have known how to make and use the claimed oligonucleotides because, as discussed briefly in the interview, each of the claimed oligonucleotides is defined structurally, in that it comprises at least a specified portion of SEQ ID NO:1, and functionally, in that it selectively hybridizes to at least three nucleotides 5' and 3' to the specified position.

In summary, it is submitted that the specification clearly would have enabled one skilled in the art to make and use the compositions of claims 10 to 21 without undue experimentation. Accordingly, it is respectfully requested that the objection to the specification and corresponding rejection of claims 10 to 21 under 35 U.S.C. § 112, first paragraph, be removed.

In view of the amendments and the above remarks, it is submitted that the claims are in condition for allowance and a notice to that effect is respectfully requested. The Examiner is invited to contact Applicants' undersigned representative if there are any questions relating to this application.

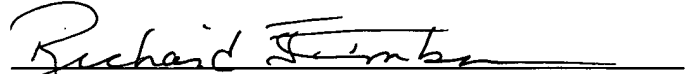
In the Application of:  
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Respectfully submitted,

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Richard J. Imbra  
Reg. No. 37,643  
Telephone: (858) 677-1496  
Facsimile: (858) 677-1465

**CUSTOMER NUMBER 28213**  
**GRAY CARY WARE & FREIDENRICH LLP**  
4365 Executive Drive, Suite 1100  
San Diego, California 92121-2133  
**USPTO CUSTOMER No. 28213**

Exhibits A, B and C